REMARKS

Reconsideration is requested.

Claims 1-23 are pending.

Claim 23 has been added to recite the details of claim 3 with the specific indication of the open reading frames. No new matter has been added.

The specification has been amended to include a complete Sequence Listing. The attached paper and computer readable copies of the Sequence Listing are the same. No new matter has been added. A separate Letter to this effect is attached.

The applicants elect, with traverse, the subject matter of Group I (claim 1, 4-9, 13 and 17) for further prosecution in the above. Reconsideration and withdrawal of the restriction requirement are requested in view of the following comments.

Claims 12 and 21 have been amended above for clarity, however, the applicants respectfully submit the claims as originally presented were clear.

The applicants respectfully submit the claimed subject matter is directed to a single invention. Withdrawal of the restriction requirement and examination of all the claims are requested.

At a minimum, the applicants submit that the subject matter of the Examiner's Groups I, II and III should be combined and examined in this application and the Examiner is requested to indicate that the combined subject matter of the Examiner's Groups IV and V is directed to an independent and distinct invention. Moreover, in the event the subject matter of Groups I, II and III are combined, the applicants respectfully submit that the subject matter of Groups IV and V should be rejoined, at an appropriate time, pursuant to the Commissioner's Notice which was

published at 1184 OG 86 on March 26, 1996, as well as the TRAINING MATERIALS FOR TREATMENT OF PRODUCT AND PROCESS CLAIMS IN LIGHT OF *IN RE BROUWER* AND *IN RE OCHIAI* AND 35 U.S.C. 103(b), U.S. Patent and Trademark Office, Office of Patent Policy Dissemination, Patent Academy rev. 7/25/96. Sufficient notice and time to amend the method claims for rejoinder is also requested, at an appropriate time.

The subject matter of Groups I, II and III should be combined and examined together because the Examiner's only basis for restricting the claims is an allegation that the inventions are distinct, based on their "different classification." See, page 3 of the Office Action of September 12, 2000 (Paper No. 12). The Examiner has also indicated, however, that a search of the claims of Groups I, II and III involves a search of the same art, i.e., class 435, subclass 325.1. See, page 2 of Paper No. 12. Similarly, the subject matter of Groups IV and V are indicated by the Examiner to be classified in the same class 435, subclass 5. Accordingly, by the Examiner's own admission, these "inventions" are not distinct for the reasons provided and have not acquired a separate status in the art as shown by their identical classification. Withdrawal of the restriction requirement is therefor requested.

In the event the restriction requirement is maintained, the applicants request further clarification as to how the claims define separate and patentably distinct inventions. Specifically, the Examiner's reference to "materially different methods" on page 3 of Paper No. 12 is not understood. The Examiner is requested to see, for example, pages 11-14 of the present specification which provides additional methods to detect variance. These methods include, for instance, the use of antibodies to detect escape mutants. Clarification is requested in the event the restriction requirement is maintained.

In event the Examiner refuses to rejoin all the claims and withdraw the restriction requirement, or combine the subject matter of Groups I -III and IV-V, the Examiner is requested to examine claims 1, 3, 4-9, 12-13, 17 and 23 in Group I. The applicants respectfully submit that claim 1 encompasses all Pol mutations, including Pol mutations resulting in other changes in HBsAg. Claim 3 also includes a mutation to an open reading frame, such as Pol. The applicants submit the linking technical feature between claims 1, 2 and 3 are key mutations in the polymerase and/or the surface component, which results in the desired changes. When the mutations relates to the translation product of Pol only, the resulting changes are the reduced sensitivity to a nucleoside analog. When the mutations concern the surface component only, the mutations result in HBV variance with a decreased interactivity of immunological reagents to the viral surface components. In the case that there is a mutation in the translation products of both Pol and the surface component, the resulting virus will have a reduced sensitivity to a nucleoside analog and a decreased interactivity of immunological reagents to the viral surface components. The applicants submit claim 1 encompasses the requirements of claim 3 such that, at a minimum, claims 1, 3-9, 12-13, 17 and 23 should be examined together.

For the Examiner's convenience, the applicants note that all the mutations specifically listed in claim 12 refer to mutations in the B domain and/or C domain of HBV DNA polymerase or a region proximal thereto. This is clear from SEQ ID NO: 29, Figure 4 and pages 4-5 of the specification. The term proximal thereto is further defined, for example, at page 6, lines 13-14 of the specification. Examples 4-7 relate to such changes in the DNA polymerase in relation to treatments with nucleoside analogs. The Examiner is also requested to appreciate that the particular part of the polymerase described above overlaps with part of the surface component. Specifically, position 499 of the polymerase corresponds to position 144-145 of the surface

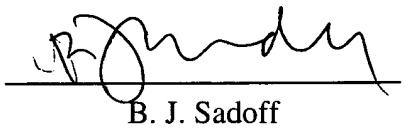
component and position 559 of the polymerase corresponds to positions 204-205 of the surface components. The applicants submit it is clear from pages 9, lines 22-25 that amino acid residue numbers 118 to 169 and/or also 169 to 207 of the surface antigen are contemplated in the present invention. The Examiner is also requested to see, for example, page 7, lines 9-10, page 16, lines 3-4, page 24, lines 21-22 and example 8 of the present specification. Moreover, one of ordinary skill in the art will be able to make and use mutations in the polymerase which affect the surface component, from the present teaching and a reasonable amount of experimentation.

Reconsideration and withdrawal of the restriction requirement are requested. The Examiner is requested to contact the undersigned for the purpose of arranging an interview, at a time convenient for the Examiner, if, after consideration of the above, the Examiner continues to believe the original restriction requirement should be maintained.

The undersigned notes, pursuant to the "Changes To Implement The Patent Business Goals", Federal Register, Vol. 65, No. 175, Friday, September 8, 2000, 54604-54683, 54637, that the above form of amending the specification and claims is proper. The Examiner is requested to contact the undersigned if anything further is required in this regard.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

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